

REMARKS

This is in further response to the Final Office Action mailed June 26, 2003 and Applicants' telephone interview with Examiner J. A. Goldberg on October 28, 2003. Claims 2-3, 7-12, 23, 34 and 36-42 have been canceled. Claims 1, 4-6, 13-22, 24, 33 and 35 are now pending.

Independent claim 1 as amended in Applicants' Amendment filed on Nov. 26, 2003 specifies a method for detecting mutation of HBV in a sample using a pair of specifically designed primers having SEQ ID NOs: 1 and 2, and particularly for detecting a mutation at amino acid position 130, 131, 133 or 145, or mutations at amino acid positions 130 and 145, 130 and 133, 131 and 145, or 133 and 145.

During Applicants' telephone interview with the Examiner on Oct. 28, 2003, the Examiner stated that the pending claims would be allowable if Applicants submit a declaration showing that the primer set SEQ ID NO:1 / SEQ ID NO:2 does something different than that resulted by using a primer set in the prior art, e.g., being able to identify mutants that are not be able to be identified by the primer set used in the prior art.

In the Amendment filed on Nov. 26, 2003, Applicants objected to the Examiner's assertion of "functional equivalents" as to the primer set SEQ ID NO:1/SEQ ID NO:2 and pointed out the Office's lack of sound legal and factual grounds for rejecting the claims under 35 §U.S.C. 103(a). However, to expedite the prosecution, Applicants submit herewith a declaration under 37 C.F.R. §1.132 signed by Dr. Chong Jin Oon, a co-inventor of the instant application. Also submitted is Dr. Oon's curriculum vitae showing that he is a prominent and productive scientist and expert in the fields of HBV virology and genomics.

As stated in Dr. Oon's declaration, Dr. Oon's laboratory has conducted experiments comparing the ability of different primer sets to identify HBV mutants in samples collected from individuals, especially those HBV strains that have escaped hepatitis B vaccination and/or resist antiviral therapy. Leveraging their many years of experience in studying the HBV genome and mining their proprietary database of HBV variants, Dr. Oon's scientific research team has specifically designed the PCR primers of SEQ ID NO: 1 and SEQ ID NO: 2 and compared the results with those obtained by PCR using a different pair of primer: MD 14 and HD03

(previously described in Oon et al. "Molecular epidemiology of Hepatitis B virus vaccine variants in Singapore" Vaccine (1995), Vol.13, No:8, pp 699-702, and in Harrison T.J. et al . "Independent emergence of a vaccine-induced escape of HepatitiB mutant of Hepatitis B virus" Journal of Hepatology (1991) 13(Suppl.4), S105-107, which were submitted to the Examiner in the IDS mailed March 25, 2003).

The data described in Dr. Oon's declaration demonstrate that the primer pair SEQ ID NO:1 / SEQ ID NO:2 are superior to the primer pair MD 14 /HD03. The primer pair MD 14 /HD03 disclosed in the prior art references are unable to detect a variety of HBsAg surface mutants. In contrast, the primer pair SEQ ID NO:1/SEQ ID NO:2 are able to detect various HBV Surface antigen negative, but PCR positive HBV viruses, such as the Glycine145Arginine, Glycine130Aspartate, Proline120Serine, and Threonine131Proline mutants.

In view of the distinct structural and functional differences between the primer set of SEQ ID NO:1/SEQ ID NO:2 and that disclosed in the prior art, Applicants further establish that the claimed invention is not only novel but also non-obvious under 35 §U.S.C. 103(a). Withdrawal of this ground of rejection and allowance of the pending are again respectively requested.

Appl. No. 09/870,358
Supplemental Communication dated Dec. 10, 2003
Reply to Office Action of November 5, 2003


CONCLUSION

Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit Examiner to expedite prosecution of this patent application to issuance. Should Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

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Date: Dec. 10, 2003


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